

AMENDMENTS TO THE CLAIMS

The following claim listing is meant to replace all previous claim listings.

1. (Withdrawn) A method for the design and/or the selection of chemokines variants having agonist or antagonist property towards a ligand of GPCR of animal cells comprising the following steps:

- A) obtaining a phage displayed library expressing on their surface said chemokine variants mutated within the domain responsible for their effector function,
- B) having a culture of animal cells expressing on their membranes the GPCR,
- C) Incubating the cell culture with the phage library obtained In A),
- D) harvesting the cells after removal of non specifically bond and surface receptor bound phages,
- E) Releasing the phages internalized in step C) by lysis of cells obtained in D)
- F) Infecting an *E. coli* culture with the released phages obtained in E) and amplifying the clones previously internalized ,
- G) Obtaining a phage library enriched in internalizing chemokines ligands,
- H) Assaying the agonist or antagonist property of the chemokine variants versus the native one.

2. (Withdrawn) The method according to claim 1 wherein the chemokine is RANTES.

3. (Withdrawn) The method according to claim 1 wherein the GPCR expressed within the membrane of animal cells is CCR5.

4. (Withdrawn) The method according to claim 1 wherein the animal cells are human cells.

5. (Withdrawn) The method according to claim 2 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- a. Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- b. Performing a PCR mutagenesis of the 5' portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- c. Inserting the purified PCR products into a phage display vector,
- d. Production of the phage library by introducing the vector containing the purified PCR products into an *E. coli* culture.

6. (Withdrawn) The method according to claim 2 wherein anti-HIV activity is assayed.

7. (Withdrawn) A method for the design and/or the selection of chemokines having agonist or antagonist property towards a GPCR of animal cells comprising the following steps:

- i. obtaining a phage displayed library expressing on their surface said chemokine mutated within the domain responsible for their effector function,
- ii. having a culture of animal cells expressing on their membranes the GPCR,
- iii. Incubating the cell culture with the phage library obtained in A),
- iv. Eliminating the non specifically bound phages from the cells, by a process keeping the specifically bound phages on the said receptor

- v. Incubating the cells obtained in D) with an *E. coli* culture and amplifying the clones being infected by the phages bound to the said receptor on animal cells,
- vi. Obtaining a phage library enriched in externally bound phages,
- vii. Assaying the agonist or antagonist property of the chemokine variants versus the native chemokine.

8. (Withdrawn) The method according to claim 7 wherein the chemokine is RANTES.

9. (Withdrawn) The method according to claim 7 wherein the GPCR expressed within the membrane of animal cells is CCR5.

10. (Withdrawn) The method according to claim 7 wherein the animal cells are human cells.

11. (Withdrawn) The method according to claim 8 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- a. Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- b. Performing a PCR mutagenesis of the 5'portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- c. Inserting the purified PCR products into a phage display vector,
- d. Production of the phage library by introducing the vector containing the purified PCR products into an *E. coli* culture.

12. (Withdrawn) The method according to claim 8 wherein anti-HIV activity is assayed.

13. (Currently Amended) A compound obtainable by a method according to anyone of ~~claims 1 to 12 of~~ comprising the following formula: ~~*XaaSP#Xaa&&& Xaa, Xaa, Xaa~~ (SEQ ID NO:40) in which

- a. ~~*~~ Xaa at position 1 is L or an aromatic residue,
- b. ~~#~~ Xaa at position 4 is L, M ~~ou~~ or V
- c. ~~&~~ Xaa at position 8-10 is S, P, T or A.

14. (Currently Amended) The compound according to claim 13 having one of the following formulae :

| | |
|------------|----------------------------------|
| LSPVSSQSSA | (SEQ ID NO: 1) (P ₁) |
| FSPLSSQSSA | (SEQ ID NO: 2) (P ₂) |
| LSPMSSQSPA | (SEQ ID NO: 3) |
| WSPLSSQSPA | (SEQ ID NO: 4) |
| WSPLSSQSSP | (SEQ ID NO: 5) |
| LSPQSSLSSS | (SEQ ID NO: 6) |
| ASSGSSQSTS | (SEQ ID NO: 7) |
| ISAGSSQSTS | (SEQ ID NO: 8) |
| RSPMSSQSSP | (SEQ ID NO: 9) |
| YSPSSSLAPA | (SEQ ID NO: 10) |
| MSPLSSQASA | (SEQ ID NO: 11) |
| ASPMSSQSSS | (SEQ ID NO: 12) |
| QSPLSSQAST | (SEQ ID NO: 13) |

~~QSPLSSTASS (SEQ ID NO: 14)~~
~~LSPLSSQSAA (SEQ ID NO: 15)~~
~~GSSSSSQTPA (SEQ ID NO: 16)~~
~~YSPLSSQSSP (SEQ ID NO: 17)~~
~~FSSVSSQSSS, (SEQ ID NO: 18)~~
~~VSTLSSPAST, (SEQ ID NO: 30)~~
~~ASSFSSRAPP, (SEQ ID NO: 31)~~
~~QSSASSSSSA (SEQ ID NO: 32)~~
~~QSPGSSWSAA, (SEQ ID NO: 33)~~
~~QSPSSWSSS, (SEQ ID NO: 34)~~
~~QSPLSSFTSS, (SEQ ID NO: 35)~~
~~LSPQSSLSSS, (SEQ ID NO: 6)~~
~~ASPQSSLPAA, (SEQ ID NO: 36)~~
~~(1) LSPVSSQSSA (SEQ ID NO: 1)~~

15. (Withdrawn) The compound according to claim 13 having the formula:
 FSPLSSQSSA(SEQ ID N): 2-RANTES(10-68).

16. (Withdrawn) The compound according to claim 13 having the formula:
 LSPVSSQSSA-RANTES (10-68).

17. (Currently Amended) A pharmaceutical composition which comprises of a compound having the formula: *XaaSP#Xaa&&& Xaa, Xaa, Xaa (SEQ ID NO:40) in which

- * Xaa at position 1 is L or an aromatic residue,
- # Xaa at position 4 is L, M or V
- & Xaa at position 8-10 is S, P, T or A.

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

18. (Withdrawn) The composition of claim 17 in which the compound have the formula: LSPVSSQSSA(SEQ ID NO: 1)- RANTES(10-68).

19. (Withdrawn) The composition of claim 17 in which the compound have the formula: FSPLSSQSSA (SEQ ID NO:2) -RANTES-(10-68).

20. (Withdrawn) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 18.

21. (Withdrawn) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 19.

22. (Withdrawn)A method for preventing and/or curing inflammatory or malignant diseases in humans comprising a step of treatment with a composition of claim 13 or 14.

Please add the following new claims:

23. (New) A compound comprising one of the following formulae :

| | |
|------------|------------------|
| LSPQSSLSSS | (SEQ ID NO: 6), |
| ASSGSSQSTS | (SEQ ID NO: 7), |
| ISAGSSQSTS | (SEQ ID NO: 8), |
| RSPMSSQSSP | (SEQ ID NO: 9), |
| YSPSSLAPA | (SEQ ID NO: 10), |

MSPLSSQASA (SEQ ID NO: 11),
ASPMSSQSSS (SEQ ID NO: 12),
QSPLSSQAST (SEQ ID NO: 13),
QSPLSSTASS (SEQ ID NO: 14),
GSSSSSQTPA (SEQ ID NO: 16),
FSSVSSQSSS, (SEQ ID NO: 18),
VSTLSSPAST, (SEQ ID NO: 30) ,
ASSFSSRAPP, (SEQ ID NO: 31),
QSSASSSSSA (SEQ ID NO: 32),
QSPGSSWSAA, (SEQ ID NO: 33),
QSPSSWSSS, (SEQ ID NO: 34),
QSPLSSFTSS, (SEQ ID NO: 35) and
ASPQSSLPAA, (SEQ ID NO: 36).

24. (New) A compound consisting essentially of one of the following formulae :

LSPQSSLSSS (SEQ ID NO: 6),
ASSGSSQSTS (SEQ ID NO: 7),
ISAGSSQSTS (SEQ ID NO: 8),
RSPMSSQSSP (SEQ ID NO: 9),
YSPSSLAPA (SEQ ID NO: 10),
MSPLSSQASA (SEQ ID NO: 11),
ASPMSSQSSS (SEQ ID NO: 12),
QSPLSSQAST (SEQ ID NO: 13),
QSPLSSTASS (SEQ ID NO: 14),
GSSSSSQTPA (SEQ ID NO: 16),
FSSVSSQSSS, (SEQ ID NO: 18),

VSTLSSPAST, (SEQ ID NO: 30),
ASSFSSRAPP, (SEQ ID NO: 31),
QSSASSSSSA (SEQ ID NO: 32),
QSPGSSWSAA, (SEQ ID NO: 33),
QSPSSWSSS, (SEQ ID NO: 34),
QSPLSSFTSS, (SEQ ID NO: 35) and
ASPQSSLPAA, (SEQ ID NO: 36).

25. (New) A pharmaceutical composition which comprises one of the following formulae:

LSPQSSLSSS (SEQ ID NO: 6),
ASSGSSQSTS (SEQ ID NO: 7),
ISAGSSQSTS (SEQ ID NO: 8),
RSPMSSQSSP (SEQ ID NO: 9),
YSPSSSLAPA (SEQ ID NO: 10),
MSPLSSQASA (SEQ ID NO: 11),
ASPMSSQSSS (SEQ ID NO: 12),
QSPLSSQAST (SEQ ID NO: 13),
QSPLSSTASS (SEQ ID NO: 14),
GSSSSSQTPA (SEQ ID NO: 16),
FSSVSSQSSS, (SEQ ID NO: 18),
VSTLSSPAST, (SEQ ID NO: 30),
ASSFSSRAPP, (SEQ ID NO: 31),
QSSASSSSSA (SEQ ID NO: 32),
QSPGSSWSAA, (SEQ ID NO: 33),
QSPSSWSSS, (SEQ ID NO: 34),
QSPLSSFTSS, (SEQ ID NO: 35) and
ASPQSSLPAA, (SEQ ID NO: 36).

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

26. (New) A pharmaceutical composition consisting essentially of one of the following formulae:

| | |
|-------------|---------------------|
| LSPQSSLSSS | (SEQ ID NO: 6), |
| ASSGSSQSTS | (SEQ ID NO: 7), |
| ISAGSSQSTS | (SEQ ID NO: 8), |
| RSPMSSQSSP | (SEQ ID NO: 9), |
| YSPSSSLAPA | (SEQ ID NO: 10), |
| MSPLSSQASA | (SEQ ID NO: 11), |
| ASPMSSQSSS | (SEQ ID NO: 12), |
| QSPLSSQAST | (SEQ ID NO: 13), |
| QSPLSSTASS | (SEQ ID NO: 14), |
| GSSSSSQTPA | (SEQ ID NO: 16), |
| FSSVSSQSSS, | (SEQ ID NO: 18), |
| VSTLSSPAST, | (SEQ ID NO: 30), |
| ASSFSSRAPP, | (SEQ ID NO: 31), |
| QSSASSSSSA | (SEQ ID NO: 32), |
| QSPGSSWSAA | (SEQ ID NO: 33), |
| QSPPSSWSSS, | (SEQ ID NO: 34), |
| QSPLSSFTSS, | (SEQ ID NO: 35) and |
| ASPQSSLPAA, | (SEQ ID NO: 36). |

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.